

2627
64. (New)

2423
A method in accordance with claim 61, wherein said administering is topical.

2728
65. (New)

2423
A method in accordance with claim 61, wherein said administering is parenteral.

506 29
66. (New)

37889
A compound of any of claims 1, 2, 4, 8, 43, and 44, wherein said compound is a modulator of PPAR γ .

2930
67. (New)

2928
A compound of claim 66, wherein said modulator has an IC₅₀ less than 1 μ M.--

REMARKS

I. Status of the Claims:

Claims 3, 9-42, 45 and 54 are canceled herein without prejudice. Claims 1, 2, 4, 5, 8, 46, 47, and 52 are amended. Claims 55-67 are newly presented for examination. After entry of the above amendments, claims 1, 2, 4-8, 43, 44, 46-53, and 55-67 will be pending.

II. The Amendments to the Claims:

Claim 1 is amended to replace "aryl" with "benzothiazolyl." This amendment limits the scope of the claim to the elected subject matter. This subject matter is supported in the specification at p. 17, lines 30-32.

Claim 1 is further amended to recite the proviso that "when Ar¹ is-2-benzothiazolyl, X is (S(O)_k." Support for this proviso is found in the specification at p. 17, lines 30-32.

Claim 1 is further amended to delete the single bond from the Markush group for the Y substituent.

Claim 2 is amended to delete non-elected subject matter. This deletion adds no new matter. Support is found in original claim 2 and in the specification at p. 3, lines 25-26.

Claims 4 and 5 are amended to change their dependency from canceled claim 3 to claim 1.

Claim 8 is amended to substitute "benzothiazolyl" for the first recital of "phenyl." This amendment corrects the antecedent basis given the above amendment to claim 1, the base claim of claim 8.

Claims 46 and 47 are each amended to insert the term "one" after "any." This amendment places the claims in a proper multiple dependency format. Claims 46 and 47 are each also amended to delete recital of the claims canceled herein.

Claim 47 is further amended to replace the recital of "modulating conditions associated with metabolic or inflammatory disorders" with the recital of "treating a condition mediated by PPAR γ ." This subject matter finds support in the specification at p. 2, lines 28-29 and p. 9, lines 23-24. This subject matter is also supported by original claim 54.

New claim 55 is drawn "to a method in accordance with claim 47, wherein said condition is a metabolic disorder or an inflammatory condition." Support for the "metabolic disorder" subject matter is found in the specification at p. 9, lines 32-34 and support for the "inflammatory condition" subject matter is found at p. 9, lines 27-31.

New claim 56 is drawn to methods of treating and recites the conditions "NIDDM, obesity, hypertension, hyperlipidemia, hypercholesterolemia, and hyperlipoproteinemia." Support for this subject matter is found in the specification at p. 9, lines 24-27 and 32-34.

New claim 61 is drawn to a method of treating a condition selected from the group consisting of rheumatoid arthritis and atherosclerosis by administering a compound of the recited formula. Support for this subject matter can be found in the specification at p. 9, lines 27-31.

New claims 57-60 and 62-65 recite host or route of administration subject matter which find support in the original claims as indicated in the following table:

New claim	Supporting original claim
57, 62	48
58, 63	49
59, 64	50
60, 65	53

New claim 66 recites "wherein said compound is a modulator of PPAR γ ." Support for this subject matter is found throughout the specification, including p. 2, last three lines.

New claim 67 depends from claim 66 and recites "wherein said modulator has an IC₅₀ less than 1 μ M." Support for this subject matter is found in Example 373 at p. 197 wherein compounds of the invention are grouped according to IC₅₀ values, including less than 1 μ M.

The proposed amendments add no new matter. Applicants respectfully request their entry.

III. Response to Rejection of Claims 46-54 under 35 U.S.C. §112, Second Paragraph

Claims 46-54 have been rejected under 35 U.S.C. §112, second paragraph, for the asserted reason that the claims are ambiguous. The above amendments to claims 46 and 47 render the rejection moot.

Applicants respectfully request that the above rejection of claims 46-54 be reconsidered and withdrawn.

IV. Rejection of Claim 52 under 35 U.S.C. §112, Second Paragraph

Claim 52 was rejected as being allegedly ambiguous with respect to the recital of "other lipid mediated diseases." In accordance with the Examiner's suggestion, claim 52 has been amended to recite:

52. (Amended) A method in accordance with claim 55, wherein said condition is selected from the group consisting of NIDDM, obesity, hypercholesterolemia, hyperlipidemia, hyperlipoproteinemia, and inflammatory conditions.

Applicants respectfully request that the above rejection of claim 52 be reconsidered and withdrawn.

V. Rejection of Claims 47-54 under 35 U.S.C. §112, first paragraph

Claims 47-54 stand rejected as allegedly containing subject matter which is not enabled.

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Without acquiescing to the allegation, but in the interest of expediting prosecution of the application, Applicants have amended Claims 47-54 to recite "A method for treating a condition mediated by PPAR γ in a host. . . "

The prior art teaches PPAR γ modulation for the treatment of conditions mediated by PPAR γ , e.g., conditions characterized by inappropriate (e.g., less or greater than normal) PPAR γ activity. For example, Lehmann et al. (1995) J. Biol. Chem. 270:12953-12956 (incorporated by reference. . .) teaches that PPAR γ modulation of activation modulates adipocyte differentiation and is useful for treating diabetes. Applicants disclose methods for evaluating the PPAR γ -modulating activity of a compound (see page 26, line 6 to page 25, line 17) and methods for formulating and administering PPAR γ -modulating compounds and compositions (see page 25, line 20 to page 27, line 21). Illustrative examples of evaluation of selected compounds of the invention *in vitro* (see, Example 373 at page 197) and evaluation of selected compounds of the invention in an *in vivo* model of a PPAR γ -mediated condition (see, Example 374 at page 198) are provided.

In light of the teachings of the prior art and the disclosure, Applicants submit that skilled artisan would be able to make and use the presently claimed compounds and compositions to treat a PPAR γ -mediated condition in a host without undue experimentation. As such, Applicants respectfully request that the rejection be reconsidered and withdrawn.

VI. Rejection of Claims 1-54 as being allegedly anticipated under 35 U.S.C. §102(b)/§103(a)

Claims 1-54 stand rejected under 35 U.S.C. §102(b) as allegedly being anticipated by Heinz et al. (U.S. Patent No. 5,814,646), Reel et al. (U.S. Patent No. 5,624,937), Cox et al. (U.S. Patent No. 4,852,419) and Cox et al. (U.S. Patent No. 4,900,751).

Claims 1-54 also stand rejected as allegedly being obvious under 35 U.S.C. §103(a) over Heinz et al. (U.S. Patent No. 5,814,646), Reel et al. (U.S. Patent No. 5,624,937), Cox et al. (U.S. Patent No. 4,852,419) and Cox et al. (U.S. Patent No. 4,900,751).

MPEP §2131 requires that to anticipate a claim, the reference must teach every element of the claim.

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A. The Heinz et al. reference (U.S. Patent No. 5,814,646).

Heinz et al. fail to teach every element of claim 1 and therefore can not anticipate claims 1-54. Heinz et al. disclose aryl ureas and thioureas as inhibitors of amyloid beta-protein production. In particular, Heinz et al. teach compounds of formula I, e.g., RN-190331-20-5. The compounds of Heinz et al. formula I contain a urea or a thiourea linkage. The presently claimed compounds do not contain such a urea or thiourea linkage. *See*, for example, the definition of substituent Y in instant claim 1. Further, there is no suggestion or motivation in Heinz et al. to make the compounds of claim 1.

In light of the above, Applicants respectfully request that the above rejection of claims 1-54 over Heinz et al. be reconsidered and withdrawn.

B. The Reel et al. Reference (U.S. Patent No. 5,624,937).

Reel et al. disclose phenyl ureas and thioureas, e.g., RN 1190331-20-5 as inhibitors of amyloid beta protein production. For the reasons cited above, Applicants respectfully request that the rejections be reconsidered and withdrawn.

C. Cox et al. References (U.S. Patents Nos. 4,900,751 and 4,852,419).

The Cox et al. patents disclose benzothiazole derivatives having anti-inflammatory or gastric acid secretion activity. In particular, the references teach 2-pyridinyl-phenylsulphonyl- and 2-pyridinyl-phenylthiobenzthiazolyl derivatives, e.g., RN 112903-43-2. The amendments to claim 1 render this rejection moot.

Applicants therefore request that any such rejection of claims 1-54 under 35 U.S.C. §103(a) be reconsidered and withdrawn.

CONCLUSION

In view of the foregoing, Applicants believe all claims now pending in this Application are in condition for allowance. The issuance of a formal Notice of Allowance at an early date is respectfully requested.

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If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at 925-472-5000.

Respectfully submitted,



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VERSION WITH MARKINGS TO SHOW CHANGES MADE

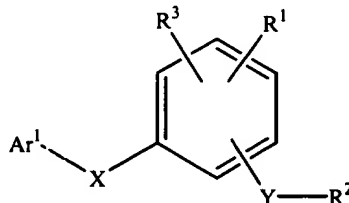
In the claims:

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Claims 3, 9-42, 45, and 54 are canceled.

Claims 1, 2, 4, 5, 8, 46, 47 and 52 are to be amended as follows:

1. (Amended) A compound having the formula:



wherein

Ar¹ is a substituted or unsubstituted [aryl] benzothiazolyl;

X is a divalent linkage selected from the group consisting of (C₁-C₆)alkylene, (C₁-C₆)alkylenoxy, (C₁-C₆)alkylenamino, (C₁-C₆)alkylene-S(O)_k-, -O-, -C(O)-, -N(R¹¹)-, -N(R¹¹)C(O)-, -S(O)_k- and a single bond,

wherein

R¹¹ is a member selected from the group consisting of hydrogen, (C₁-C₈)alkyl, (C₂-C₈)heteroalkyl and aryl(C₁-C₄)alkyl; and the subscript k is an integer of from 0 to 2;

Y is a divalent linkage selected from the group consisting of alkylene, -O-, -C(O)-, -N(R¹²)-S(O)_m-, -N(R¹²)-S(O)_m-N(R¹³)-, -N(R¹²)C(O)-, and -S(O)_n- [and a single bond],

wherein

R¹² and R¹³ are members independently selected from the group consisting of hydrogen, (C₁-C₈)alkyl, (C₂-C₈)heteroalkyl and aryl(C₁-C₄)alkyl; and the subscripts m and n are independently integers of from 0 to 2;

R¹ is a member selected from the group consisting of hydrogen, (C₂-C₈)heteroalkyl, aryl, aryl(C₁-C₄)alkyl, halogen, cyano, nitro, (C₁-C₈)alkyl, (C₁-C₈)alkoxy, -C(O)R¹⁴, -CO₂R¹⁴, -C(O)NR¹⁵R¹⁶, -S(O)_p-R¹⁴, -S(O)_q-NR¹⁵R¹⁶, -O-C(O)-OR¹⁷, -O-C(O)-R¹⁷, -O-C(O)-NR¹⁵R¹⁶, -N(R¹⁴)-C(O)-NR¹⁵R¹⁶, -N(R¹⁴)-C(O)-R¹⁷ and -N(R¹⁴)-C(O)-OR¹⁷;

wherein

R¹⁴ is a member selected from the group consisting of hydrogen, (C₁-C₈)alkyl, (C₂-C₈)heteroalkyl, aryl and aryl(C₁-C₄)alkyl;

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R^{15} and R^{16} are members independently selected from the group consisting of hydrogen, (C_1-C_8) alkyl, (C_2-C_8) heteroalkyl, aryl, and aryl (C_1-C_4) alkyl, or taken together with the nitrogen to which each is attached form a 5-, 6- or 7-membered ring;

R^{17} is a member selected from the group consisting of (C_1-C_8) alkyl, (C_2-C_8) heteroalkyl, aryl and aryl (C_1-C_4) alkyl;

the subscript p is an integer of from 0 to 3; and

the subscript q is an integer of from 1 to 2; and

R^2 is a substituted or unsubstituted aryl; and

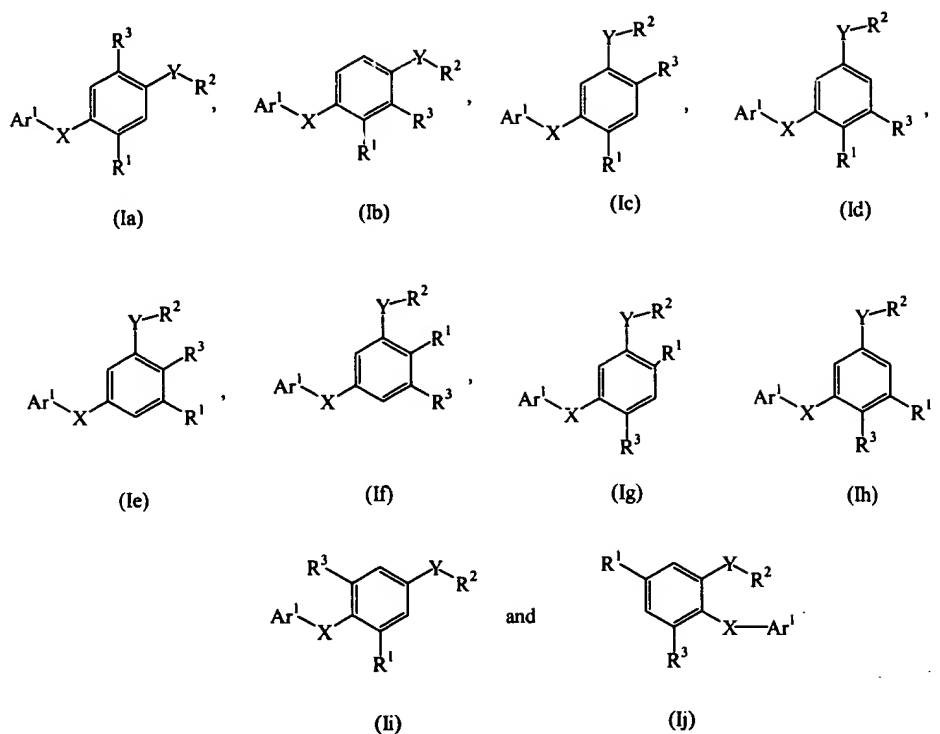
R^3 is a member selected from the group consisting of halogen, cyano, nitro and (C_1-C_8) alkoxy[.],

with the proviso that when Ar^1 is 2-benzothiazolyl, X is $S(O)_k$.

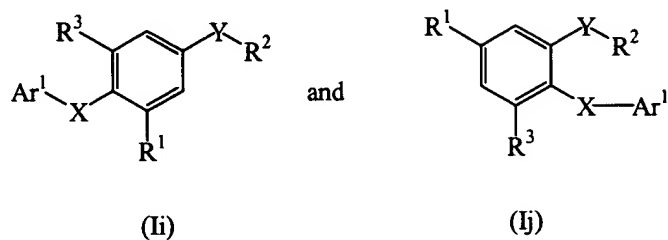
2. (Amended) A compound of claim 1, wherein [Ar^1 is a substituted or unsubstituted aryl selected from the group consisting of pyridyl, phenyl, naphthyl, isoquinolinyl, benzthiazolyl, benzoxazolyl and benzimidazolyl; with the proviso that when Ar^1 is substituted or unsubstituted benzthiazolyl, then X is $-S(O)_k$; and] R^2 is a substituted or unsubstituted aryl selected from the group consisting of phenyl, pyridyl, naphthyl and pyridazinyl.

4. (Amended) A compound of claim [3] 1, represented by a formula selected from the group consisting of

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5. (Amended) A compound of claim [3] 1, represented by a formula selected from the group consisting of



8. (Amended) A compound of claim 7, wherein Ar¹ is a [phenyl] benzothiazolyl group having from 1 to 3 substituents selected from the group consisting of halogen, -OCF₃, -OH, -O(C₁-C₆)alkyl, -CF₃, (C₁-C₈)alkyl and -NO₂; R¹ is a member selected from the group consisting of halogen, (C₁-C₃)alkyl, (C₂-C₈)heteroalkyl and (C₁-C₈)alkoxy; R² is a phenyl group having from 0 to 3 substituents selected from the group consisting of halogen, -OCF₃, -OH, -O(C₁-C₈)alkyl, -C(O)-(C₁-C₈)alkyl, -CN, -CF₃, (C₁-C₈)alkyl and -NH₂; and R³ is selected from the group consisting of halogen, methoxy and trifluoromethoxy.

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46. (Amended) A composition comprising a pharmaceutically acceptable excipient and a compound of any one of claims [1-45] 1, 2, 4-8, 43, and 44.

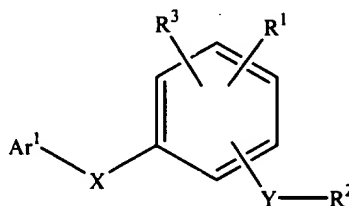
47. (Amended) A method for [modulating conditions associated with metabolic or inflammatory disorders] treating a condition mediated by PPAR γ in a host, said method comprising administering to said host an efficacious amount of a compound of any one of claims [1-45] 1, 2, 4-8, 43, and 44.

52. (Amended) A method in accordance with claim [47] 55, wherein said [disorders are] condition is selected from the group consisting of NIDDM, obesity, hypercholesterolemia [and other lipid-mediated diseases], hyperlipidemia, hyperlipoproteinemia, and inflammatory conditions.

Claims 55-67 have been added as follows:

55. (New) A method in accordance with claim 47, wherein said condition is a metabolic disorder or an inflammatory condition.

56. (New) A method of treating a condition selected from the group consisting of NIDDM, obesity, hypertension, hyperlipidemia, hypercholesterolemia, and hyperlipoproteinemia in a host, said method comprising administering to said host an efficacious amount of a compound of formula:



wherein

Ar¹ is a substituted or unsubstituted benzothiazolyl;

X is a divalent linkage selected from the group consisting of (C₁-C₆)alkylene, (C₁-C₆)alkylenoxy, (C₁-C₆)alkylenamino, (C₁-C₆)alkylene-S(O)_k-, -O-, -C(O)-, -N(R¹¹)-, -N(R¹¹)C(O)-, -S(O)_k- and a single bond,

wherein

R¹¹ is a member selected from the group consisting of hydrogen, (C₁-

C_8 alkyl, (C_2-C_8) heteroalkyl and aryl(C_1-C_4)alkyl; and the subscript k is an integer of from 0 to 2;

Y is a divalent linkage selected from the group consisting of alkylene, -O-, -C(O)-, -N(R¹²)-S(O)_m-, -N(R¹²)-S(O)_m-N(R¹³)-, -N(R¹²)C(O)-, and -S(O)_n-,

wherein

R¹² and R¹³ are members independently selected from the group consisting of hydrogen, (C_1-C_8) alkyl, (C_2-C_8) heteroalkyl and aryl(C_1-C_4)alkyl; and the subscripts m and n are independently integers of from 0 to 2;

R¹ is a member selected from the group consisting of hydrogen, (C_2-C_8) heteroalkyl, aryl, aryl(C_1-C_4)alkyl, halogen, cyano, nitro, (C_1-C_8) alkyl, (C_1-C_8) alkoxy, -C(O)R¹⁴, -CO₂R¹⁴, -C(O)NR¹⁵R¹⁶, -S(O)_p-R¹⁴, -S(O)_q-NR¹⁵R¹⁶, -O-C(O)-OR¹⁷, -O-C(O)-R¹⁷, -O-C(O)-NR¹⁵R¹⁶, -N(R¹⁴)-C(O)-NR¹⁵R¹⁶, -N(R¹⁴)-C(O)-R¹⁷ and -N(R¹⁴)-C(O)-OR¹⁷;

wherein

R¹⁴ is a member selected from the group consisting of hydrogen, (C_1-C_8) alkyl, (C_2-C_8) heteroalkyl, aryl and aryl(C_1-C_4)alkyl;

R¹⁵ and R¹⁶ are members independently selected from the group consisting of hydrogen, (C_1-C_8) alkyl, (C_2-C_8) heteroalkyl, aryl, and aryl(C_1-C_4)alkyl, or taken together with the nitrogen to which each is attached form a 5-, 6- or 7-membered ring;

R¹⁷ is a member selected from the group consisting of (C_1-C_8) alkyl, (C_2-C_8) heteroalkyl, aryl and aryl(C_1-C_4)alkyl;

the subscript p is an integer of from 0 to 3; and

the subscript q is an integer of from 1 to 2; and

R² is a substituted or unsubstituted aryl; and

R³ is a member selected from the group consisting of halogen, cyano, nitro and (C_1-C_8) alkoxy,

with the proviso that when Ar¹ is 2-benzothiazolyl, X is S(O)_k.

57. (New) A method in accordance with claim 56, wherein said host is a mammal selected from the group consisting of humans, dogs, monkeys, mice, rats, horses and cats.

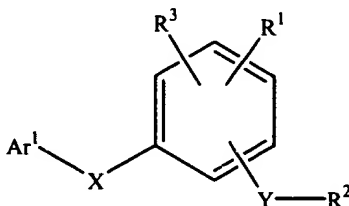
58. (New) A method in accordance with claim 56, wherein said administering is oral.

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59. (New) A method in accordance with claim 56, wherein said administering is topical.

60. (New) A method in accordance with claim 56, wherein said administering is parenteral.

61. (New) A method of treating a condition selected from the group consisting of rheumatoid arthritis and atherosclerosis in a host, said method comprising administering to said host, an efficacious amount of a compound of formula:



wherein

Ar¹ is a substituted or unsubstituted benzothiazolyl;

X is a divalent linkage selected from the group consisting of (C₁-C₆)alkylene, (C₁-C₆)alkylenoxy, (C₁-C₆)alkylenamino, (C₁-C₆)alkylene-S(O)_k-, -O-, -C(O)-, -N(R¹¹)-, -N(R¹¹)C(O)-, -S(O)_k- and a single bond,

wherein

R¹¹ is a member selected from the group consisting of hydrogen, (C₁-C₈)alkyl, (C₂-C₈)heteroalkyl and aryl(C₁-C₄)alkyl; and the subscript k is an integer of from 0 to 2;

Y is a divalent linkage selected from the group consisting of alkylene, -O-, -C(O)-, -N(R¹²)-S(O)_m-, -N(R¹²)-S(O)_m-N(R¹³)-, -N(R¹²)C(O)-, and -S(O)_n-,

wherein

R¹² and R¹³ are members independently selected from the group consisting of hydrogen, (C₁-C₈)alkyl, (C₂-C₈)heteroalkyl and aryl(C₁-C₄)alkyl; and the subscripts m and n are independently integers of from 0 to 2;

R¹ is a member selected from the group consisting of hydrogen, (C₂-C₈)heteroalkyl, aryl, aryl(C₁-C₄)alkyl, halogen, cyano, nitro, (C₁-C₈)alkyl, (C₁-C₈)alkoxy, -C(O)R¹⁴, -CO₂R¹⁴, -C(O)NR¹⁵R¹⁶, -S(O)_p-R¹⁴, -S(O)_q-NR¹⁵R¹⁶, -O-C(O)-OR¹⁷, -O-C(O)-R¹⁷, -O-C(O)-NR¹⁵R¹⁶, -N(R¹⁴)-C(O)-NR¹⁵R¹⁶, -N(R¹⁴)-C(O)-R¹⁷ and -N(R¹⁴)-C(O)-OR¹⁷;

wherein

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R^{14} is a member selected from the group consisting of hydrogen, (C_1-C_8) alkyl, (C_2-C_8) heteroalkyl, aryl and aryl (C_1-C_4) alkyl;

R^{15} and R^{16} are members independently selected from the group consisting of hydrogen, (C_1-C_8) alkyl, (C_2-C_8) heteroalkyl, aryl, and aryl (C_1-C_4) alkyl, or taken together with the nitrogen to which each is attached form a 5-, 6- or 7-membered ring;

R^{17} is a member selected from the group consisting of (C_1-C_8) alkyl, (C_2-C_8) heteroalkyl, aryl and aryl (C_1-C_4) alkyl;

the subscript p is an integer of from 0 to 3; and

the subscript q is an integer of from 1 to 2; and

R^2 is a substituted or unsubstituted aryl; and

R^3 is a member selected from the group consisting of halogen, cyano, nitro and (C_1-C_8) alkoxy,

with the proviso that when Ar^1 is 2-benzothiazolyl, X is $S(O)_k$.

62. (New) A method in accordance with claim 61, wherein said host is a mammal selected from the group consisting of humans, dogs, monkeys, mice, rats, horses and cats.

63. (New) A method in accordance with claim 61, wherein said administering is oral.

64. (New) A method in accordance with claim 61, wherein said administering is topical.

65. (New) A method in accordance with claim 61, wherein said administering is parenteral.

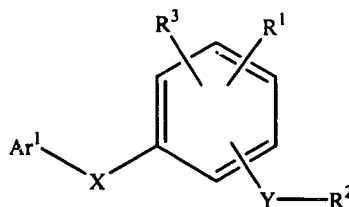
66. (New) A compound of any of claims 1, 2, 4-8, 43, and 44, wherein said compound is a modulator of $PPAR\gamma$.

67. (New) A compound of claim 66, wherein said modulator has an IC_{50} less than 1 μM .

APPENDIX 1

PENDING CLAIMS FOLLOWING ENTRY OF THIS AMENDMENT

1. (Amended) A compound having the formula:



wherein

Ar¹ is a substituted or unsubstituted benzothiazolyl;

X is a divalent linkage selected from the group consisting of (C₁-C₆)alkylene, (C₁-C₆)alkylenoxy, (C₁-C₆)alkylenamino, (C₁-C₆)alkylene-S(O)_k-, -O-, -C(O)-, -N(R¹¹)-, -N(R¹¹)C(O)-, -S(O)_k- and a single bond,

wherein

R¹¹ is a member selected from the group consisting of hydrogen, (C₁-C₈)alkyl, (C₂-C₈)heteroalkyl and aryl(C₁-C₄)alkyl; and the subscript k is an integer of from 0 to 2;

Y is a divalent linkage selected from the group consisting of alkylene, -O-, -C(O)-, -N(R¹²)-S(O)_m-, -N(R¹²)-S(O)_m-N(R¹³)-, -N(R¹²)C(O)-, and -S(O)_n-,

wherein

R¹² and R¹³ are members independently selected from the group consisting of hydrogen, (C₁-C₈)alkyl, (C₂-C₈)heteroalkyl and aryl(C₁-C₄)alkyl; and the subscripts m and n are independently integers of from 0 to 2;

R¹ is a member selected from the group consisting of hydrogen, (C₂-C₈)heteroalkyl, aryl, aryl(C₁-C₄)alkyl, halogen, cyano, nitro, (C₁-C₈)alkyl, (C₁-C₈)alkoxy, -C(O)R¹⁴, -CO₂R¹⁴, -C(O)NR¹⁵R¹⁶, -S(O)_p-R¹⁴, -S(O)_q-NR¹⁵R¹⁶, -O-C(O)-OR¹⁷, -O-C(O)-R¹⁷, -O-C(O)-NR¹⁵R¹⁶, -N(R¹⁴)-C(O)-NR¹⁵R¹⁶, -N(R¹⁴)-C(O)-R¹⁷ and -N(R¹⁴)-C(O)-OR¹⁷;

wherein

R¹⁴ is a member selected from the group consisting of hydrogen, (C₁-C₈)alkyl, (C₂-C₈)heteroalkyl, aryl and aryl(C₁-C₄)alkyl;

R¹⁵ and R¹⁶ are members independently selected from the group consisting

of hydrogen, (C₁-C₈)alkyl, (C₂-C₈)heteroalkyl, aryl, and aryl(C₁-C₄)alkyl, or taken together with the nitrogen to which each is attached form a 5-, 6- or 7-membered ring;

R¹⁷ is a member selected from the group consisting of (C₁-C₈)alkyl, (C₂-C₈)heteroalkyl, aryl and aryl(C₁-C₄)alkyl;

the subscript p is an integer of from 0 to 3; and

the subscript q is an integer of from 1 to 2; and

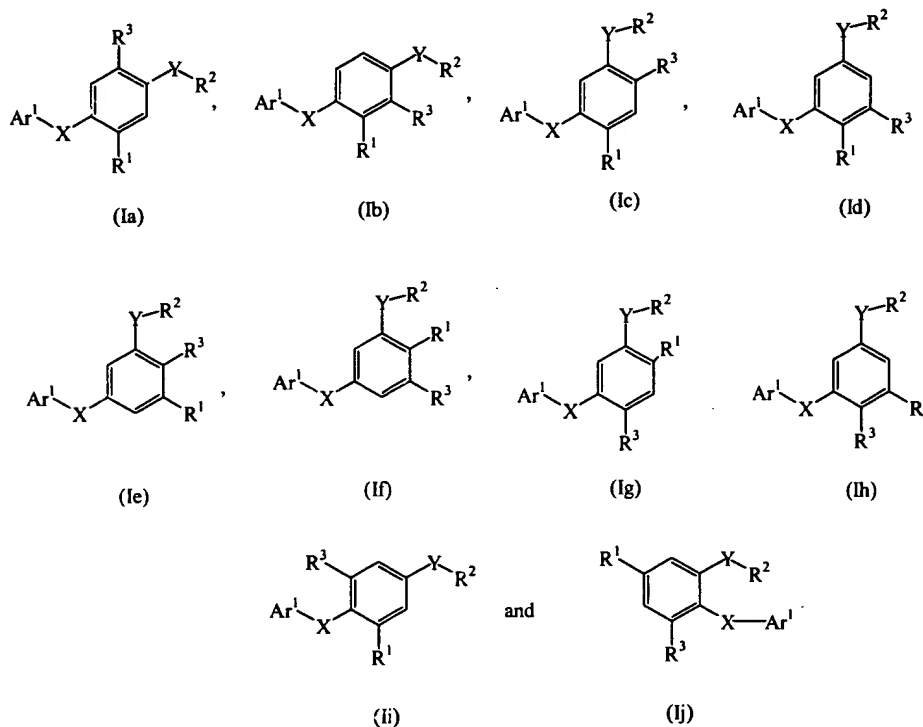
R² is a substituted or unsubstituted aryl; and

R³ is a member selected from the group consisting of halogen, cyano, nitro and (C₁-C₈)alkoxy,

with the proviso that when Ar¹ is 2-benzothiazolyl, X is S(O)_k.

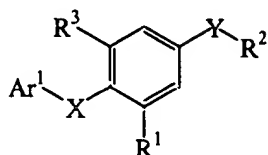
2. (Amended) A compound of claim 1, wherein R² is a substituted or unsubstituted aryl selected from the group consisting of phenyl, pyridyl, naphthyl and pyridazinyl.

4. (Amended) A compound of claim 1, represented by a formula selected from the group consisting of



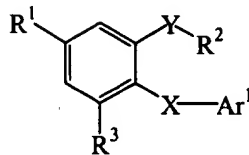
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5. (Amended) A compound of claim 1, represented by a formula selected from the group consisting of



(Ii)

and



(Ij)

6. A compound of claim 5, wherein

X is a divalent linkage selected from the group consisting of $-\text{CH}_2-$, $-\text{CH}(\text{CH}_3)-$, $-\text{O}-$, $-\text{C}(\text{O})-$, $-\text{N}(\text{R}^{11})-$ and $-\text{S}-$;

wherein

R^{11} is a member selected from the group consisting of hydrogen and $(\text{C}_1-\text{C}_8)\text{alkyl}$;

Y is a divalent linkage selected from the group consisting of $-\text{N}(\text{R}^{12})-\text{S}(\text{O})_2-$,

wherein

R^{12} is a member selected from the group consisting of hydrogen and $(\text{C}_1-\text{C}_8)\text{alkyl}$;

R^1 is a member selected from the group consisting of hydrogen, halogen, $(\text{C}_1-\text{C}_8)\text{alkyl}$, $(\text{C}_2-\text{C}_8)\text{heteroalkyl}$, $(\text{C}_1-\text{C}_8)\text{alkoxy}$, $-\text{C}(\text{O})\text{R}^{14}$, $-\text{CO}_2\text{R}^{14}$, $-\text{C}(\text{O})\text{NR}^{15}\text{R}^{16}$, $-\text{S}(\text{O})_p-\text{R}^{14}$, $-\text{S}(\text{O})_q-\text{NR}^{15}\text{R}^{16}$, $-\text{O}-\text{C}(\text{O})-\text{R}^{17}$, and $-\text{N}(\text{R}^{14})-\text{C}(\text{O})-\text{R}^{17}$;

wherein

R^{14} is a member selected from the group consisting of hydrogen, $(\text{C}_1-\text{C}_8)\text{alkyl}$, $\text{hetero}(\text{C}_1-\text{C}_8)\text{alkyl}$, aryl and $\text{aryl}(\text{C}_1-\text{C}_4)\text{alkyl}$;

R^{15} and R^{16} are members independently selected from the group consisting of hydrogen, $(\text{C}_1-\text{C}_8)\text{alkyl}$ and $(\text{C}_2-\text{C}_8)\text{heteroalkyl}$, or taken together with the nitrogen to which each is attached form a 5-, 6- or 7-membered ring;

R^{17} is a member selected from the group consisting of hydrogen, $(\text{C}_1-\text{C}_8)\text{alkyl}$ and $(\text{C}_2-\text{C}_8)\text{heteroalkyl}$;

the subscript p is an integer of from 0 to 2; and

the subscript q is 2; and

R^2 is a substituted or unsubstituted phenyl; and

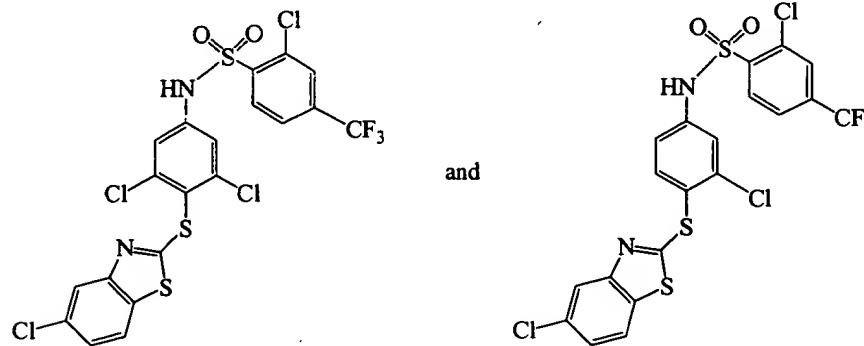
R^3 is a member selected from the group consisting of halogen and $(\text{C}_1-\text{C}_8)\text{alkoxy}$.

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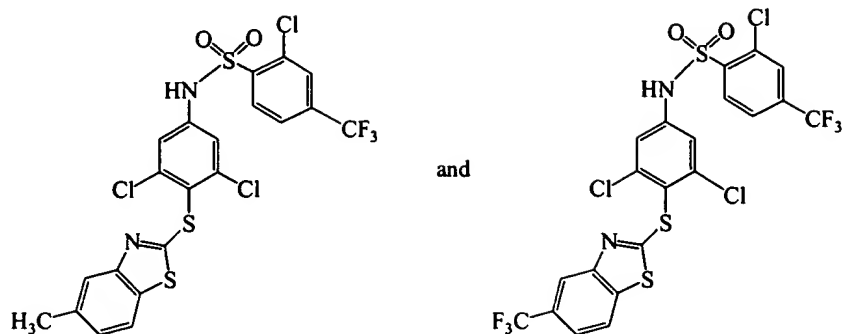
7. A compound of claim 6, wherein X is -O-, -NH- or -S-; Y is -NH-SO₂-; R¹ is a member selected from the group consisting of halogen, (C₁-C₈)alkyl, (C₂-C₈)heteroalkyl, (C₁-C₈)alkoxy, -C(O)R¹⁴, -CO₂R¹⁴, -C(O)NR¹⁵R¹⁶, -S(O)_p-R¹⁴ and -S(O)_q-NR¹⁵R¹⁶; R² is a phenyl group having from 0 to 3 substituents selected from the group consisting of halogen, -OCF₃, -OH, -O(C₁-C₈)alkyl, -C(O)-(C₁-C₈)alkyl, -CN, -CF₃, (C₁-C₈)alkyl and -NH₂; and R³ is selected from the group consisting of halogen, methoxy and trifluoromethoxy.

8. (Amended) A compound of claim 7, wherein Ar¹ is a benzothiazolyl group having from 1 to 3 substituents selected from the group consisting of halogen, -OCF₃, -OH, -O(C₁-C₆)alkyl, -CF₃, (C₁-C₈)alkyl and -NO₂; R¹ is a member selected from the group consisting of halogen, (C₁-C₈)alkyl, (C₂-C₈)heteroalkyl and (C₁-C₈)alkoxy; R² is a phenyl group having from 0 to 3 substituents selected from the group consisting of halogen, -OCF₃, -OH, -O(C₁-C₈)alkyl, -C(O)-(C₁-C₈)alkyl, -CN, -CF₃, (C₁-C₈)alkyl and -NH₂; and R³ is selected from the group consisting of halogen, methoxy and trifluoromethoxy.

43. A compound of claim 1, selected from the group consisting of:



44. A compound of claim 1, selected from the group consisting of:



46. (Amended) A composition comprising a pharmaceutically acceptable excipient and a compound of any one of claims 1, 2, 4-8, 43, and 44.

47. (Amended) A method for treating a condition mediated by PPAR γ in a host, said method comprising administering to said host an efficacious amount of a compound of any one of claims 1, 2, 4-8, 43, and 44.

48. A method in accordance with claim 47, wherein said host is a mammal selected from the group consisting of humans, dogs, monkeys, mice, rats, horses and cats.

49. A method in accordance with claim 47, wherein said administering is oral.

50. A method in accordance with claim 47, wherein said administering is topical.

51. A method in accordance with claim 47, wherein said administering is prophylactic to prevent the onset of a PPAR γ -mediated condition.

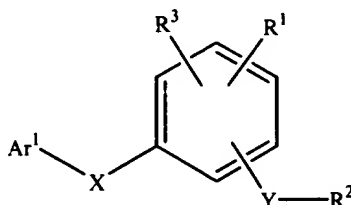
52. (Amended) A method in accordance with claim 55, wherein said condition is selected from the group consisting of NIDDM, obesity, hypercholesterolemia, hyperlipidemia, hyperlipoproteinemia, and inflammatory conditions.

53. A method in accordance with claim 47, wherein said administering is parenteral.

55. (New) A method in accordance with claim 47, wherein said condition is a metabolic disorder or an inflammatory condition.

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56. (New) A method of treating a condition selected from the group consisting of NIDDM, obesity, hypertension, hyperlipidemia, hypercholesterolemia, and hyperlipoproteinemia in a host, said method comprising administering to said host an efficacious amount of a compound of formula:



wherein

Ar^1 is a substituted or unsubstituted benzothiazolyl;

X is a divalent linkage selected from the group consisting of (C₁-C₆)alkylene, (C₁-C₆)alkylenoxy, (C₁-C₆)alkylenamino, (C₁-C₆)alkylene-S(O)_k-, -O-, -C(O)-, -N(R¹¹)-, -N(R¹¹)C(O)-, -S(O)_k- and a single bond,

wherein

R¹¹ is a member selected from the group consisting of hydrogen, (C₁-C₈)alkyl, (C₂-C₈)heteroalkyl and aryl(C₁-C₄)alkyl; and the subscript k is an integer of from 0 to 2;

Y is a divalent linkage selected from the group consisting of alkylene, -O-, -C(O)-, -N(R¹²)-S(O)_m-, -N(R¹²)-S(O)_m-N(R¹³)-, -N(R¹²)C(O)-, and -S(O)_n-,

wherein

R¹² and R¹³ are members independently selected from the group consisting of hydrogen, (C₁-C₈)alkyl, (C₂-C₈)heteroalkyl and aryl(C₁-C₄)alkyl; and the subscripts m and n are independently integers of from 0 to 2;

R¹ is a member selected from the group consisting of hydrogen, (C₂-C₈)heteroalkyl, aryl, aryl(C₁-C₄)alkyl, halogen, cyano, nitro, (C₁-C₈)alkyl, (C₁-C₈)alkoxy, -C(O)R¹⁴, -CO₂R¹⁴, -C(O)NR¹⁵R¹⁶, -S(O)_p-R¹⁴, -S(O)_q-NR¹⁵R¹⁶, -O-C(O)-OR¹⁷, -O-C(O)-R¹⁷, -O-C(O)-NR¹⁵R¹⁶, -N(R¹⁴)-C(O)-NR¹⁵R¹⁶, -N(R¹⁴)-C(O)-R¹⁷ and -N(R¹⁴)-C(O)-OR¹⁷;

wherein

R¹⁴ is a member selected from the group consisting of hydrogen, (C₁-C₈)alkyl, (C₂-C₈)heteroalkyl, aryl and aryl(C₁-C₄)alkyl;

R¹⁵ and R¹⁶ are members independently selected from the group consisting of hydrogen, (C₁-C₈)alkyl, (C₂-C₈)heteroalkyl, aryl, and aryl(C₁-

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C₄)alkyl, or taken together with the nitrogen to which each is attached form a 5-, 6- or 7-membered ring;

R¹⁷ is a member selected from the group consisting of (C₁-C₈)alkyl, (C₂-C₈)heteroalkyl, aryl and aryl(C₁-C₄)alkyl;

the subscript p is an integer of from 0 to 3; and

the subscript q is an integer of from 1 to 2; and

R² is a substituted or unsubstituted aryl; and

R³ is a member selected from the group consisting of halogen, cyano, nitro and (C₁-C₈)alkoxy,

with the proviso that when Ar¹ is 2-benzothiazolyl, X is S(O)_k.

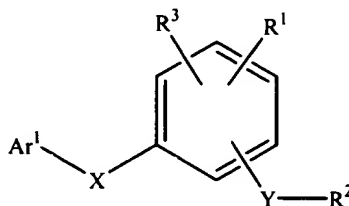
57. (New) A method in accordance with claim 56, wherein said host is a mammal selected from the group consisting of humans, dogs, monkeys, mice, rats, horses and cats.

58. (New) A method in accordance with claim 56, wherein said administering is oral.

59. (New) A method in accordance with claim 56, wherein said administering is topical.

60. (New) A method in accordance with claim 56, wherein said administering is parenteral.

61. (New) A method of treating a condition selected from the group consisting of rheumatoid arthritis and atherosclerosis in a host, said method comprising administering to said host, an efficacious amount of a compound of formula:



wherein

Ar¹ is a substituted or unsubstituted benzothiazolyl;

X is a divalent linkage selected from the group consisting of (C₁-C₆)alkylene, (C₁-C₆)alkylenoxy, (C₁-C₆)alkylenamino, (C₁-C₆)alkylene-S(O)_k-, -O-, -C(O)-, -N(R¹¹)-, -N(R¹¹)C(O)-, -S(O)_k- and a single bond,

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wherein

R^{11} is a member selected from the group consisting of hydrogen, (C_1-C_8) alkyl, (C_2-C_8) heteroalkyl and aryl (C_1-C_4) alkyl; and the subscript k is an integer of from 0 to 2;

Y is a divalent linkage selected from the group consisting of alkylene, -O-, -C(O)-, -N(R^{12})-S(C)_m-, -N(R^{12})-S(O)_m-N(R^{13})-, -N(R^{12})C(O)-, and -S(O)_n-,

wherein

R^{12} and R^{13} are members independently selected from the group consisting of hydrogen, (C_1-C_8) alkyl, (C_2-C_8) heteroalkyl and aryl (C_1-C_4) alkyl; and the subscripts m and n are independently integers of from 0 to 2;

R^1 is a member selected from the group consisting of hydrogen, (C_2-C_8) heteroalkyl, aryl, aryl (C_1-C_4) alkyl, halogen, cyano, nitro, (C_1-C_8) alkyl, (C_1-C_8) alkoxy, -C(O) R^{14} , -CO₂ R^{14} , -C(O)NR¹⁵ R^{16} , -S(O)_p- R^{14} , -S(O)_q-NR¹⁵ R^{16} , -O-C(O)-OR¹⁷, -O-C(O)- R^{17} , -O-C(O)-NR¹⁵ R^{16} , -N(R^{14})-C(O)-NR¹⁵ R^{16} , -N(R^{14})-C(O)- R^{17} and -N(R^{14})-C(O)-OR¹⁷;

wherein

R^{14} is a member selected from the group consisting of hydrogen, (C_1-C_8) alkyl, (C_2-C_8) heteroalkyl, aryl and aryl (C_1-C_4) alkyl;

R^{15} and R^{16} are members independently selected from the group consisting of hydrogen, (C_1-C_8) alkyl, (C_2-C_8) heteroalkyl, aryl, and aryl (C_1-C_4) alkyl, or taken together with the nitrogen to which each is attached form a 5-, 6- or 7-membered ring;

R^{17} is a member selected from the group consisting of (C_1-C_8) alkyl, (C_2-C_8) heteroalkyl, aryl and aryl (C_1-C_4) alkyl;

the subscript p is an integer of from 0 to 3; and

the subscript q is an integer of from 1 to 2; and

R^2 is a substituted or unsubstituted aryl; and

R^3 is a member selected from the group consisting of halogen, cyano, nitro and (C_1-C_8) alkoxy,

with the proviso that when Ar¹ is 2-benzothiazolyl, X is S(O)_k.

62. (New) A method in accordance with claim 61, wherein said host is a mammal selected from the group consisting of humans, dogs, monkeys, mice, rats, horses and cats.

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63. (New) A method in accordance with claim 61, wherein said administering is oral.

64. (New) A method in accordance with claim 61, wherein said administering is topical.

65. (New) A method in accordance with claim 61, wherein said administering is parenteral.

66. (New) A compound of any of claims 1, 2, 4-8, 43, and 44, wherein said compound is a modulator of PPAR γ .

67. (New) A compound of claim 66, wherein said modulator has an IC₅₀ less than 1 μ M.

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